Applicants submit one of ordinary skill in the art would understand that where a substituent is not clearly indicated on an atom which is a member of a ring and which has capacity for an additional covalent bond, a hydrogen atom would normally be present. Applicants further submit that such designations of chemical compounds are conventional in the art (for example, benzene). Additionally, one of skill in the art *also* understands that a hydrogen atom would not be present when another substituent or an additional covalent bond takes the place of the hydrogen.

For example, as stated in the specification at page 12, lines 23-27: "[t]hose skilled in the art will appreciate that the double bonds illustrated in Formula VII are included therein to represent that the moieties have aromatic character, *and* that these double bonds may shift for certain substituents, in particular for =O and NH_2 at positions 2 and 4, in order for the moiety to retain its aromatic character" (emphasis added).

Given 1) the statements set forth above and the overt statement in the specification at page 12 regarding the variable position of a double bond, and 2) the knowledge of one of ordinary skill in the art, Formula VII as defined in the claims does embrace cytosine because one of skill in the art would understand that the double bonds of the moiety generally set forth by Formula VII may shift for the moiety to retain its aromatic character.

In the moiety at issue in this particular rejection, namely cytosine (as described at the bottom of page 2 of the Office Action), one of ordinary skill in the art would understand that to the extent the nitrogen at position 3 is "unavailable" due to the presence of the double bond between positions 3 and 4, there would be no hydrogen substituent at position 3. In the other state, i.e., when the nitrogen at position 3 is "available," then there would be hydrogen at position 3. Accordingly, because one of skill in the art would know whether a hydrogen is present as a substituent on the moiety and the position of the hydrogen atom, if any, based on the position of the double bond in Formula VII, applicants respectfully request withdrawal of the rejection.

Claim 68 also stands rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Office Action indicates cytosine is a pyrimidinyl moiety where the 4 position is substituted by a $-NH_2$, moiety and the bond between the 3 and 4 position is a double bond,

which is not embraced by the pyrimidinyl moiety of formula VII in claim 56. Applicants respectfully traverse the rejection.

As indicated above, the specification (as well as claim 56) contemplates the presence of a double bond between the 3 and 4 positions on the pyrimidinyl moiety generally described as Formula VII. Additionally, applicants have indicated on page 12, line 28 of the instant specification, they consider cytosine a pyrimidinyl moiety within the scope of what is referred to as a "pyrimidinyl moiety" in the claims. By clearly specifying cytosine in the list of possible "B" substituents in the specification at page 12, line 27-29, applicants have affirmatively asserted that cytosine is a pyrimidinyl moiety embraced by the pyrimidinyl moiety of formula VII in claim 56. Consistent with the description in the specification at page 12, lines 23-27, cytosine's double bond is merely shifted relative to Formula VII, in order for the moiety to retain its aromatic character.

Accordingly, because cytosine is a pyrimidinyl moiety within the scope of claim 56, applicants respectfully request withdrawal of the rejection to claim 68 because the claim is also allowable by virtue of its dependency upon claim 56, which embraces the pyrimidinyl moiety cytosine.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 101 stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and/or use the invention. The Office Action indicates the great diversity of diseases falling within the "tumor" category means that it is contrary to medical understanding that any agent could be generally effective against such diseases. The Office Action then asserted *In re Buting* 163 U.S.P.Q. 689 (1969) to support its position. Applicants respectfully traverse the rejection.

1. The Case Law Cited by the Office is Irrelevant to Enablement

First, applicants submit the Office's reliance on *In re Buting* is misplaced. In that case, the sole question for review was whether the demonstrated evidence of efficacy was sufficient under **35 U.S.C. § 101** to support an allegation of utility in humans. The claims at issue were directed to seven specific types of cancer, and the claim at issue in that case listed each type of

cancer in a Markush group. Thus, the types of cancer specified were limitations of the claims at issue. The court indicated the evidence provided by the applicant was not commensurate with the broad scope of **utility** claimed. The reasoning by the court was provided solely because the cancers set forth in the claims were limitations of the claims. At no point does the case address enablement requirements, let alone the factors set forth in *In re Wands*, 858 F.2d 731, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988), the seminal case on the issue of enablement.

Accordingly, because the Office Action is improperly relying on a case that is irrelevant for the purpose for which it is offered, and that irrelevant purpose is the primary support for the rejection, applicants respectfully request withdrawal of the rejection.

2. The Claimed Invention is Enabled

If, however, the Office continues to assert the claimed method is not enabled, applicants respectfully submit that one of skill in the art can make and use the invention without undue experimentation.

Applicants have found that the compounds of the invention have anti-cancer activity (see, e.g., page 15, lines 9-11) and have disclosed in the specification manners of carrying out the method of the invention to treat cancers.

The Office Action asserts that it is contrary to medical understanding that any agent could be generally effective against all forms of cancer. Applicants respectfully disagree. All forms of cancer share certain characteristics, e.g., they result from cells that grow and divide quickly. Therefore, an agent which inhibits cells that grow and divide quickly will have usefulness in treating cancers. So, e.g., chemical agents like paclitaxel are effective to some degree against cancers in general. The fact that such agents are not approved by the Food and Drug Administration (FDA) or widely used within the oncology community for treating all forms of cancer does not mean that they are not at some level useful against cancer in general. The standard for enablement under the patent law is not FDA approval or commercial success. See, *In re Brana,* 51 F.3d 1560, 34 U.S.P.Q. 1436 (Fed. Cir. 1995).

Furthermore, to the extent that experimentation is required to determine the specific cancers which are optimally treated by the method of the invention, such experimentation would not be undue. In other words, the proper test for enablement is: "If any experimentation is

necessary to practice the invention, is that experimentation undue or unreasonable?" The court in *In re Wands* discussed a number of factors to determine whether a disclosure was sufficient to enable one of ordinary skill in the art to practice the invention throughout its scope without having to engage in undue experimentation. Some factors to be considered are: 1) the quantity of experimentation, 2) the amount of guidance presented, and 3) the presence of working examples.

Here, applicants have enabled the full scope of the invention by providing guidance regarding how to make the functional "backbone" of the chemical compound (Formula III), as well as describing the possible substituents and providing the position of each substituent on the backbone.

Additionally, at page 15, lines 9-11, applicants affirmatively assert that experimentation has shown that compounds of Formula III have potent anti-tumor activity, in particular against the KB-cell line, thereby providing working examples.

Applicants submit that given the level of skill in the art and the amount of detail set forth in the specification regarding the structure of the moieties, one of ordinary skill in the art could make and use the claimed composition within the full scope of the claim. Specifically, applicants submit that one of skill in the art of oncology, or a similar field of study, would without undue experimentation, be able to determine which moieties to substitute onto Formula III that would be most effective against tumors, thereby making any experimentation that may be necessary merely routine and not undue or unreasonable.

In the absence of any evidence that the claimed method is not enabled, the Office has not met its burden. Accordingly, because applicants have taught how to carry out the method of the invention and the Office Action does not set forth evidence to support non-enablement of the claimed method, applicants submit that the method of claim 101 is enabled and respectfully request withdrawal of the rejection.

Claims 56-71 and 96 also stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is mostly nearly connected, to make and/or use the invention. The Office Action indicates the rejected claims call for the treatment of viruses generally. Applicants respectfully traverse.

Before explaining the bases for traversal, applicants note that claim 96 is dependent upon independent claim 95, which is not rejected under 35 U.S.C. § 112, first paragraph. Applicants further note that neither independent claim 95 nor claim 96 is drawn to a method of treating viruses and therefore applicants respectfully request withdrawal of the rejection of claim 96 under 35 U.S.C. § 112, first paragraph.

With respect to claims 56-71, the Office Action asserts that it is contrary to medical understanding that any agent could be generally effective against all forms of viruses. Applicants respectfully disagree. Viruses share certain characteristics; e.g., they infect cells and use cellular metabolism and "machinery" to replicate themselves. Therefore, an agent which inhibits viral replication or infection will have usefulness in treating viruses.

Applicants submit that under the test for enablement, applicants have enabled the full scope of the invention. With respect to the factors set forth in *In re Wands* and above, applicants disclose how to make the functional "backbone" (Formula III) of the chemical compound, as well as describe the possible R-group substituents and moieties as well as provide the position of each on the backbone. In other words, given the level of skill in the art and the amount of detail throughout the specification, applicants have provided sufficient guidance to enable one of ordinary skill in the art of virology or similar endeavor to make and use the claimed composition within the full scope of the claims. More specifically, applicants submit one skilled in the appropriate art would know which moieties would be most effective against a specific virus, and therefore one skilled in the appropriate art would select which moiety or moieties to conjugate with Formula III. For example, as described in the specification at page 11, lines 4-7, moiety "Z" is a moiety that has demonstrated anti-viral activity by itself. Thus, conjugation of the "Z" moiety to Formula III provides compounds that include multiple sites for viral inhibition.

In further support of applicants' position that the claims are enabled throughout their scope, the specification at page 11, line 1, through page 13, line 2, describes Formula III, as well as the various substituents in detail. Additionally, on page 14, lines 20-32 of the instant specification, applicants describe experimentation that demonstrates the efficacy of administering Formula III to combat viral infection, and in particular inhibit HIV-1 activity in CEM-SS cells. Examples 8 and 9 also demonstrate anti-viral activity against HIV-1 and HBV.

The Office Action also asserts a chapter from "Fields Virology" to support the rejection.

Applicants submit the passage cited by the Office Action does not support the rejection. Specifically, the present invention comprises a functional backbone (Formula III) with multiple moieties suitable for adaptation against multiple virus types. In the present case, applicants have shown the present invention may be used against HIV-1 activity as well as how to make and use other particular embodiments within the scope of the claims. Given the level of skill in the art, the disclosure provides many compounds that one of skill in the relevant art may tailor to inhibit molecules serving functions unique to a virus. Whether or not it is true that "the best targets for the inhibition by antiviral molecules are theoretically molecules serving a function unique to the virus," (emphasis added) (1) the standard for enablement under the patent law is not disclosing the "best" target and (2) the quoted statement itself indicates that it is only "theoretically" true.

In the absence of any evidence that one of skill in the art cannot make and use the compound set forth in the claims and administer the compounds, the claims are enabled. Accordingly, because the Office Action does not set forth any evidence to support the rejection, applicants submit the claims are enabled and respectfully request withdrawal of the rejection.

Summary

In view of the foregoing remarks, applicants submit that this application is in condition for allowance and respectfully request early and favorable notification to that effect. If it would expedite prosecution of this application, the Examiner is invited to confer with applicants' undersigned attorneys.

Respectfully submitted,
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8/23/01
(Date)

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